

JOSEPH ANTHONY FRANCISCO, Ph.D.

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PROFILE

Versatile Ph.D. research scientist with experience in biochemical engineering, antibody engineering, and preclinical evaluation of biologics for the treatment of cancer and other diseases. Extensive experience in molecular biology, protein engineering, expression, purification, and in vitro characterization of therapeutic proteins, immunoassay development, pharmacokinetic analysis, and the establishment and therapy of murine models of cancer.

EDUCATION

Ph.D. in Chemical Engineering, The University of Texas at Austin, Austin, Texas, 1994.
Dissertation: The Expression of Recombinant Proteins on the External Surface of *Escherichia coli*.

B.A. in Chemical Engineering and Biochemistry, Rice University, Houston, Texas, 1989.

EXPERIENCE

Seattle Genetics, Inc., Bothell, WA (1998-present)

Associate Director of Molecular Biology, (4/00-present)

Conduct applied research for the discovery and development of protein therapeutics for the treatment cancer and other human malignancies. Responsibilities and accomplishments include:

- Direct research activities of personnel in the molecular biology department (currently 6 research associates, 1 PhD scientist), keeping focused on company priorities and objectives.
- Function as project leader for significant priority project; establish timelines, identify and assign personnel to key functions including contract manufacturing.
- Establish and optimize a system for antibody chimerization, addressing relevant issues for producing research reagents as well as for GMP manufacturing.
- Design and supervise preclinical mouse studies to evaluate the toxicity and efficacy of chemical and recombinant protein agents.

Principal Scientist, (1998-2000)

Responsibilities and accomplishments include:

- Direct a research program to investigate the therapeutic efficacy of novel antibodies and antibody-fusions as potential anti-cancer agents. Design and conduct *in vitro* and *in vivo* experiments to study the activities of these agents.
- Establish a research program for antibody engineering.
- Supervise the research activities of four research associates.
- Functioned as project leader for a significant priority project which was successfully outlicensed to a major biotech corporate partner.
- Establish quality control assays and procedures for ongoing stability analysis of clinical-grade single-chain anti-cancer immunotoxin.

Monsanto, St. Louis, MO (1997 - 1998)

Scientist, Protein Regulatory Sciences Department.

Responsible for the purification, characterization, and safety assessment of recombinant proteins expressed in plants for agricultural and pharmaceutical purposes. Duties included the design and implementation studies to support submissions to US and foreign regulatory agencies.

Bristol-Myers Squibb Pharmaceutical Research Institute, Seattle, WA (1994 - 1997).

Research Investigator II, Molecular Immunology Department (1997).

Responsible for the construction and characterization of novel immunotoxins and antibodies for the treatment of cancer. Supervised one research associate. Accomplishments include:

- Constructed and characterized the *in vitro* activity of novel single-chain immunotoxins.
- Evaluated the therapeutic efficacy of novel antibodies (murine, chimeric, and humanized forms) *in vitro* and in murine models of human cancer.
- Developed assays to evaluate the pharmacokinetics of mAbs in mice and monkeys.
- Member of the working groups established to evaluate the therapeutic potential of targeting CD40 for the treatment of human hematologic malignancies and carcinomas.
- Member of the project working groups responsible for the transfer of a recombinant single-chain immunotoxin to bioprocess research and an outside contractor for the production of GMP material for phase I clinical trials.

Postdoctoral Fellow, Molecular Immunology Department (1994-1996).

Responsible for the engineering and characterization of single-chain immunotoxins targeted to CD40 and their evaluation as therapeutic agents for human lymphoma and multiple myeloma.

Accomplishments include:

- Constructed and characterized the *in vitro* activity of the first single-chain immunotoxin targeted to human CD40.
- Established models of human lymphoma and multiple myeloma in SCID mice to investigate the *in vivo* efficacy of antibodies and single-chain immunotoxins.
- Evaluated the toxicity and pharmacokinetics of this immunotoxin in mice, rats, and monkeys.
- Participated in the development of a single-chain anticarcinoma immunotoxin that entered phase I clinical trial.

The University of Texas at Austin, Austin, TX (1989-1994).

Graduate Research Assistant, Department of Chemical Engineering. Supervised by Professor George Georgiou.

Responsible for designing, cloning, expressing and characterizing a novel protein fusion for the stable expression of recombinant proteins on the external surface of *E. coli*. (US Patent 5,348,867). Supervised several undergraduate research assistants.

- Recipient of the Hoechst Celanese Corporation Graduate Presentation Award, 1993.
- Recipient of the Dow Centennial Fellowship, 1992.

Teaching Assistant, Department of Chemical Engineering (1993).

Course title: Introductory Biochemical Engineering

Teaching Assistant, Department of Chemical Engineering (1990).

Course title: Fundamental Chemical Engineering Laboratory.

PUBLICATIONS

Francisco, J.A., Donaldson, K.L., Chace, D., Siegall, C.B., and Wahl, A.F., "Agonistic properties and *in vivo* antitumor activity of the anti-CD40 antibody SGN-14," Cancer

- Research, 60, 3225-3231 (2000).
- Francisco, J.A. and Siegall, C.B., "Single-chain immunotoxins targeted to CD40 for the treatment of human B-lineage hematologic malignancies," Leukemia and Lymphoma, 30, 237-245 (1998).
- Francisco, J.A., Gawlak, S.L., Miller, M., Bathe, J., Russell, D., Chace, D., Mixan, B., Zhao, L., Fell, H.P., and Siegall, C.B., "Expression and characterization of Bryodin 1 and a Bryodin 1-based single-chain immunotoxin from tobacco cell culture," Bioconjugate Chemistry, 8, 708-713 (1997).
- Ledbetter, J.A., Francisco, J.A., Siegall, C.B., Gilliland, L.K., Hollenbaugh, D., Aruffo, A., Siadak, A.W., Mischel-Petty, N., Grosmaire, L.S., Gordon, M.L., Brown, T.J., Moran-Davis, P., Mittler, R.S., Kiener, P.K., and Nadler, S.G., "Agonistic activity of a CD40 specific single-chain Fv constructed from the variable regions of mAb G28-5," Critical Reviews in Immunology, 17, 427-435 (1997).
- Francisco, J.A., Gawlak, S.L., and Siegall, C.B., "Construction, expression and characterization of BD1-G28-5 sFv, a single-chain anti-CD40 immunotoxin containing the ribosome-inactivating protein bryodin 1," Journal of Biological Chemistry, 272, 24165-24169 (1997).
- Francisco, J.A., Schreiber, G.J., Comerkeski, C.R., Mezza, L.W., Warner, G.L., Davidson, T.J., Ledbetter, J.A., and Siegall, C.B., "In vivo efficacy and toxicity of a single-chain immunotoxin targeted to CD40," Blood, 89, 4493-4500 (1997).
- Francisco, J.A., Kiener, P.A., Ledbetter, J.A., and Siegall, C.B., "Cytokine activation sensitizes human monocytic and endothelial cells to the cytotoxic effects of an anti-CD40 immunotoxin," Journal of Immunology, 157, 1652-1658 (1996).
- Francisco, J.A., Gilliland, L.K., Stebbins, M.R., Norris, N.A., Ledbetter, J.A., and Siegall, C.B., "Activity of a single-chain immunotoxin that selectively kills lymphoma and other B-lineage cells expressing the CD40 antigen," Cancer Research 55, 3099-3104 (1995).
- Francisco, J.A. and Georgiou, G., "The expression of recombinant proteins on the external surface of *Escherichia coli*: biotechnological applications," Biochemical Engineering VIII: Annals of the New York Academy of Sciences, 372-382 (1994).
- Georgiou, G., Poetschke, H.L., Stathopoulos, C., and Francisco, J.A., "Practical applications of engineering Gram-negative bacterial cell surfaces," Trends in Biotechnology 11, 6-10 (1993).
- Francisco, J.A., Campbell, R., Iverson, B.L., and Georgiou, G., "Production and fluorescence activated cell sorting of *Escherichia coli* expressing a functional antibody fragment on the external surface," Proceedings of the National Academy of Science, USA 90, 10444-10448 (1993).
- Francisco, J.A., Stathopoulos, C., Warren, R.A.J., Kilburn, D.G., and Georgiou, G., "Specific adhesion and hydrolysis of cellulose by intact *Escherichia coli* expressing surface anchored cellulase or cellulose binding domains," Bio/Technology 11, 491-495 (1993).
- Francisco, J.A., Earhart, C.F., and Georgiou, G., "Transport and anchoring of β -lactamase to the external surface of *Escherichia coli*," Proceedings of the National Academy of Science, USA 89, 2713-2717 (1992).

PATENT

- Georgiou, G., Francisco, J.A., and Earhart, C.F., "Expression of Proteins on Bacterial Surface", US Patent 5,348,867 (1994).

PRESENTATIONS

- Francisco, J.A. "Molecular biology and bioconjugates," Invited speaker for Chemistry, Biology

and Applications of Bioconjugates, Short Course at the American Chemical Society annual meeting, (2000)

Francisco, J.A. "Antibody-based cancer therapeutics: Single-chain immunotoxins targeted to CD40," Invited speaker for the NIH Training Program in Biotechnology, The University of Texas at Austin (1999)

Francisco, J.A. and Siegall, C.B., "Single-chain immunotoxins as cancer chemotherapeutic agents," Antibody-Based Therapeutics: Applications and Clinical Data (1997).

Francisco, J.A., Schreiber, G.J., Warner, G.L., Davidson, T.J., Ledbetter, J.A., and Siegall, C.B., "In vitro and in vivo activity of G28-5 sFv-PE40, a single-chain immunotoxin targeted to CD40," Annual Meeting of the AACR (1997).

Francisco, J.A., Kiener, P.A., Ledbetter, J.A., Schreiber, G.J., and Siegall, C.B., "In vitro and in vivo activity of a single-chain immunotoxin targeted to CD40," Annual Meeting of the AACR (1996).

Francisco, J.A., Schreiber, G.J., Kiener, P.A., Stebbins, M.R., Ledbetter, J.A., and Siegall, C.B., "Characterization of single-chain immunotoxins targeted to CD40: antitumor activity versus B-lineage lymphoma cells," Fourth International Symposium on Immunotoxins (1995).

Francisco, J.A., Gilliland, L., Stebbins, M., Ledbetter, J.A., and Siegall, C.B., "Construction and characterization of G28-5 sFv-PE40, and anti-B cell lymphoma immunotoxin," Bristol-Myers Squibb Pharmaceutical Research Institute Fifth Annual Scientific Poster Session (1994).

Francisco, J.A., Ayling, A., Poetschke, H.L., Earhart, C.F., and Georgiou, G., "Molecular characterization of proteins expressed on the external surface of *Escherichia coli*," Annual Meeting of the ACS (1993).

PROFESSIONAL AFFILIATIONS

Member of the American Chemical Society
Member of the American Association for the Advancement of Science
Member of the American Association for Cancer Research